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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,383	09/08/2003	Yan Chang	GLYO-P03-002	9375

28120 7590 02/15/2006

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EXAMINER	
MAIER, LEIGH C	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 02/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,383	CHANG ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/8/03, 8/10/04*. 8/27/04, 11/22/04, 11/18/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 3-5, 7, 8, 13, 14 and 18-22 have been amended by pre-amendment. Claims 23-28 have been added by pre-amendment. Claim 6 has been canceled by pre-amendment. Claims 1-5 and 7-28 are pending.

Protest

It is noted that a protest was filed in this case. However, it was not timely filed and was not entered or further considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention.

The claims recite a carbohydrate that "comprises a polymeric backbone having side chains dependent therefrom." The specification discusses the use of polymeric materials, it does

not contemplate ones comprising any type of side chain, but only those terminated by a galactose or arabinose unit. See, for example, page 4 at lines 9-14. Further regarding claim 24, this claim includes the limitation that the "polymeric backbone comprises homopolymer." The examiner also finds no support for this limitation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 includes the limitation that the "polymeric backbone comprises homopolymer." It is not clear what is Applicant's intent in this claim. A "homopolymer" is a polymer comprising a single type of monosaccharide. A polymer is or is not a homopolymer—it does not comprise one. Perhaps what Applicant intends is that a backbone is composed of single type of monomer, but this is not clear, as there is no particular description of this limitation. See above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

> patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 13, 14 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Green et al (Anti-Cancer Drug Design, 1999).

Green teaches that glycoamines enhance the efficacy of taxol as an apoptotic agent in an *in vitro* system. See page 160. These glycoamines are antimetastatic agents that bind β–galactoside-specific lectins (galectins). See page 159 at the 1st full paragraph. The reference further discloses that when the article was published, that similar combination procedures *in vivo* were underway, indicating that the combination had been administered to at least an experimental patient and thus anticipating the claims. See page 161, first full paragraph.

Claims 1-4, 7, 13, 18, 20, 22-26 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Klyosov et al (US 2003/0064957).

Klyosov '957 discloses the administration of galactomannan and 5-FU by injection to mice having induced tumors. See example 3. The combination results in a synergistic effect on tumor reduction. The reference also describes the structure of galactomannan. See paragraph [0042]. This structure appears to meet the criteria of carbohydrates that would bind to galectin-1 or galectin-3. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 13, 18-26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 2003/0064957).

Klyosov '957 teaches as set forth above. The reference does not exemplify oral administration or sequential delivery of the galactomannan and oncolytic agent. However, the reference further suggests a variety of modes of administration, including oral, and sequential administration of the galactomannan and chemotherapeutic agent. See paragraphs [0032] and [0048].

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to increase the efficacy of the chemotherapeutic in the treatment of cancer with a reasonable expectation of success. The artisan would be motivated to administer this combination because the art had taught that galactomannan reduces the side effects of toxic chemotherapeutic agents. A reduction in side effects would necessarily increase the efficacy. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation.

Claims 1-4, 7, 13 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 6,645,946).

Klyosov '946 teaches the administration of galactomannan and 5-FU by injection to mice. See examples. It is noted that the mice in the examples do not actually have cancer. The reference also describes the structure of galactomannan. See paragraph bridging col 5-6. This structure appears to meet the criteria of carbohydrates that would bind to galectin-1 or galectin-3.

Although the reference does not exemplify administration to a patient having cancer, the reference specifically suggests the administration of the galactomannan/chemotherapeutic agent as a treatment for cancer. See col 2, lines 15-65. The reference teaches that the administration of the galactomannan reduces side effects produced by toxic chemotherapeutic agents. See abstract. The reference further suggests a variety of modes of administration, including oral, and sequential administration of the galactomannan and chemotherapeutic agent. See col 3, lines 35-

55, and col 4, lines 41-43 and reference claim 16. The reference is silent regarding radiation or surgical treatment.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to reduce side effects produced by the chemotherapeutic agent with a reasonable expectation of success. As noted above, the reference is silent regarding "enhanced efficacy." However, the same patient population would be treated, regardless of whether the intent was to reduce side effects or enhance efficacy. Recognition of another advantage that would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation. It would be further obvious to combine the galactomannan/chemotherapeutic treatment with other common treatments such as radiation or surgical. One of ordinary skill in the art would reasonably expect success in this combination because the use of chemotherapeutic agents in combination with radiation and/or surgery is common in the art of cancer treatment.

Claims 1-3, 13, 14 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999).

Green teaches as set forth above. The reference does not exemplify the full range of therapeutic treatments recited in the claims. However, the reference does suggest the use of the

antimetastatic glycoamines in combination with traditional therapies. See, for example, section "Anti-adhesives as chemosensitizers for ascites tumors" at page 157.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer a disclosed glycoamine in combination with any traditional therapy. It would be within the scope of the artisan to select any known therapy, such as those recited in the claim. One of ordinary skill would be motivated to combine these methods of treatment for their additive effects with a reasonable expectation of success. In preventing metastasis, the addition of the glycoamine would clearly enhance the efficacy of any other treatment. In the absence of unexpected results, it would be within the scope of the artisan to optimize the treatment protocol with respect to the timing and mode of administration through routine experimentation.

Claims 1-3, 12, 13 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin et al (US 5,639,737).

Rubin teaches that lactose or lactose conjugates of chemotherapeutic agents inhibit tumor growth and metastasis. See abstract. The reference suggests the administration of lactose or a conjugate to prevent metastases resulting from surgery, with the lactose or conjugate being administered beginning 8-12 hours prior to surgery and continuing for 3 days post-operatively. See col 14, lines 27-31.

The reference also suggests the administration of lactose alone or in combination with a lactose conjugate. See, for example, col 16, lines 33-38. In the latter case, the free lactose would correspond to the galectin-binding carbohydrate, and the conjugate would correspond to the

oncolytic chemotherapeutic. The reference further suggests the combination with other treatments. See col 17, lines 8-23. The reference is silent regarding galectin-binding, but it appears to meet the physical characteristics in that it comprises a galactose moiety, and has a molecular weight greater than the minimum contemplated.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer lactose in combination with surgery or in combination with a chemotherapeutic lactose conjugate for the treatment of cancer. One of ordinary skill would be motivated to combine these methods of treatment for their additive effects with a reasonable expectation of success. In preventing metastasis, the addition of the lactose would clearly enhance the efficacy of the surgical or chemotherapeutic treatment. In the absence of unexpected results, it would be within the scope of the artisan to optimize the treatment protocol with respect to the timing and mode of administration through routine experimentation.

Claims 1-5, 7-9, 12, 13 and 15-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of (1) Green et al (Anti-Cancer Drug Design, 1999) or (2) Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907).

Each of Green and Rubin teach the use of antimetastatic agents in combination with standard treatments for cancer. Neither reference teaches the use of modified pectin in combination with other therapeutic treatments for cancer.

Platt teaches that modified citric pectin (MCP) with molecular weight of about 10 kD has utility in the treatment and prevention of metastatic cancer. See pages 1-3 and page 6, lines 2-6.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer MCP in combination with any traditional cancer treatment. Each of Green and Rubin had taught the use of antimetastatic agents in combination with standard treatments for cancer. Therefore, one of ordinary skill would reasonably expect success in using this combination for the additive effect.

Claims 1-5, 7-10, 12, 13 and 15-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of (1) Green et al (Anti-Cancer Drug Design, 1999) or (2) Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907) and further in view of Ros et al, (Carbohyd. Res., 1996).

Green, Rubin and Platt teach as set forth above. Platt teaches the use of pH modified MCP but also specifically suggests that the citrus pectin may be modified by methods and experimental conditions known in the art may be used to prepare the MCP. See paragraph bridging pp 6-7. The reference does not exemplify citrus pectin modified enzymatically.

Ros teaches the enzymatic hydrolysis of pectin. See pp 272-3.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any method, such as enzymatic, known in the art to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Ros to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Claims 1-5, 7-9, 11-13 and 15-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of (1) Green et al (Anti-Cancer Drug Design, 1999) or (2) Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907) and further in view of Renard et al, (Carbohyd. Res., 1995).

Green, Rubin and Platt teach as set forth above. Platt teaches the use of pH modified MCP but also specifically suggests that the citrus pectin may be modified by methods and experimental conditions known in the art may be used to prepare the MCP. See paragraph bridging pp 6-7. The reference does not exemplify citrus pectin modified thermally.

Renard teaches the thermal hydrolysis of pectin. See pp 156-7, section 2.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any method known in the art, such as thermal, to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Renard to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is

appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 7-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,680,306. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of enhancing the efficacy of cancer treatment by combining a carbohydrate that binds galectin with a traditional cancer treatment. The claims of '306 are more narrowly drawn than the instant claims and would thus anticipate the instant claims.

Claims 1-5, 7-13, 15-19, 23 and 25-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 and 19-26 of U.S. Patent No. 6,690,906.

The claims of '906 are drawn to a method of treating or controlling angiogenesis or neovascularization by the administration of a carbohydrate that binds galectin. The claims do not recite the treatment of cancer or the use of the carbohydrate in combination with other treatment methods.

Zetter teaches that angiogenesis is an essential component in tumor metstasis. See abstract. Zetter also expressly suggests the administration of anti-angiogenic agents in combination with other cancer treatments. See paragraph bridging pages 417 and 418.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer the recited carbohydrate for the treatment of angiogenesis in cancer in combination with other cancer treatments for their additive effects. One of ordinary skill would reasonably expect success in such a treatment because of the teaching of Zetter. In doing so, one of ordinary skill would arrive at the instant invention.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
February 3, 2006

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